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CA INDEXING COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)

=> s eugenol
L1 21715 EUGENOL

=> s methoxyestradiol
L2 2430 METHOXYESTRADIOL

=> s l1 and l1
L3 21715 L1 AND L1

=> s l1 and l2
L4 26 L1 AND L2

=> d 14 1-26 bib abs

L4 ANSWER 1 OF 26 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2001:458743 BIOSIS
DN PREV200100458743
TI Development of novel apoptotic inducers for prostate cancer therapy.
AU Kumar, Addanki P. (1); Garcia, Gretchen E.; Rajnarayanan, Rajendram;
Alworth, William L.; Slaga, Thomas J.
CS (1) AMC Cancer Research Center, Denver, CO USA
SO Proceedings of the American Association for Cancer Research Annual
Meeting, (March, 2001) Vol. 42, pp. 448. print.
Meeting Info.: 92nd Annual Meeting of the American Association for Cancer
Research New Orleans, LA, USA March 24-28, 2001
ISSN: 0197-016X.
DT Conference
LA English
SL English

L4 ANSWER 2 OF 26 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1994:228282 BIOSIS
DN PREV199497241282
TI Reactive oxygen-dependent DNA damage resulting from the oxidation of
phenolic compounds by a copper-redox cycle mechanism.
AU Li, Yunbo; Trush, Michael A. (1)
CS (1) Dep. Environ. Health Sci., Room 7032, Johns Hopkins Sch. Hygiene
Public Health, 615 N. Wolfe St., Baltimore, MD 21205 USA
SO Cancer Research, (1994) Vol. 54, No. 7 SUPPL., pp. 1895S-1898S.
ISSN: 0008-5472.
DT Article
LA English
AB Recently, copper has been shown to be capable of mediating the activation
of several xenobiotics producing reactive oxygen and other radicals. Since
copper exists in the nucleus and is closely associated with chromosomes
and DNA bases, in this study we have investigated whether the activation
of 1,4-hydroquinone (1,4-HQ) and a variety of other phenolic compounds by
copper can induce strand breaks in double-stranded vphi-X-174 RF I DNA
(vphi-X-174 relaxed form I DNA). In the presence of micromolar
concentrations of Cu(II), DNA strand breaks were induced by 1,4-HQ and
other phenolic compounds including 4,4'-biphenol, catechol,
1,2,4-benzenetriol, 2-methoxyestradiol, 2-hydroxyestradiol,
diethylstilbestrol, butylated hydroxytoluene, butylated hydroxyanisole,
tert-butylhydroquinone, ferulic acid, caffeic acid, chlorogenic acid,
eugenol, 2-acetamidophenol, and acetaminophen. Structure-activity
analysis shows that in the presence of Cu(II), the DNA cleaving activity
for phenolic compounds with a 1,4-hydroquinone structure, such as
1,2,4-benzenetriol and tertbutylhydroquinone is greater than those with a
catechol group (catechol, 2-hydroxyestradiol and caffeic acid). Those
compounds having one phenol group, such as **eugenol**,
2-acetamidophenol, and acetaminophen, are the least reactive. In addition,
the induced DNA strand breaks could be inhibited by
bathocuproinedisulfonic acid, a Cu(I)-specific chelator, or catalase
indicating that a Cu(II)/Cu(I) redox cycle and H₂O₂ generation are two
major determinants involved in the observed DNA damage. Using reactive
oxygen scavengers, it was observed that the DNA strand breaks induced by
the 1,4-HQ/Cu(II) system could not be efficiently inhibited by hydroxyl
radical scavengers, but could be protected by singlet oxygen scavengers,
suggesting that either singlet oxygen or a singlet oxygen-like entity,
possibly a copper-peroxide complex, but not free hydroxyl radical probably
plays a role in the DNA damage. The above results would suggest that
macromolecule-associated copper and reactive oxygen generation may be
important factors in the mechanism of 1,4-HQ and other phenolic
compound-induced DNA damage in target cells.

L4 ANSWER 3 OF 26 BIOTECHNO COPYRIGHT 2002 Elsevier Science B.V.
AN 1994:24132141 BIOTECHNO
TI Reactive oxygen-dependent DNA damage resulting from the oxidation of
phenolic compounds by a copper-redox cycle mechanism
AU Li Y.; Trush M.A.

CS Environmental Health Sciences Dept., J. Hopkins Hygiene/Public Hlth.
Sch., 615 N. Wolfe Street, Baltimore, MD 21205, United States.
SO Cancer Research, (1994), 54/7 SUPPL. (1895s-1898s)
CODEN: CNREA8 ISSN: 0008-5472
DT Journal; Conference Article
CY United States

LA English
SL English

AB Recently, copper has been shown to be capable of mediating the activation of several xenobiotics producing reactive oxygen and other radicals. Since copper exists in the nucleus and is closely associated with chromosomes and DNA bases, in this study we have investigated whether the activation of 1,4- hydroquinone (1,4-HQ) and a variety of other phenolic compounds by copper can induce strand breaks in double-stranded .vphi.X-174 RF I DNA (.vphi.X-174 relaxed form I DNA). In the presence of micromolar concentrations of Cu(II), DNA strand breaks were induced by 1,4-HQ and other phenolic compounds including 4,4'-biphenol, catechol, 1,2,4-benzenetriol, 2-methoxyestradiol, 2- hydroxyestradiol, diethylstilbestrol, butylated hydroxytoluene, butylated hydroxyanisole, tert-butylhydroquinone, ferulic acid, caffeic acid, chlorogenic acid, eugenol, 2-acetamidophenol, and acetaminophen. Structure-activity analysis shows that in the presence of Cu(II), the DNA cleaving activity for phenolic compounds with a 1,4-hydroquinone structure, such as 1,2,4-benzenetriol and tert-butylhydroquinone is greater than those with a catechol group (catechol, 2-hydroxyestradiol and caffeic acid). Those compounds having one phenol group, such as eugenol, 2-acetamidophenol, and acetaminophen, are the least reactive. In addition, the induced DNA strand breaks could be inhibited by bathocuproinedisulfonic acid, a Cu(I)-specific chelator, or catalase indicating that a Cu(II)/Cu(I) redox cycle and H.sub.2O.sub.2 generation are two major determinants involved in the observed DNA damage. Using reactive oxygen scavengers, it was observed that the DNA strand breaks induced by the 1,4-HQ/Cu(II) system could not be efficiently inhibited by hydroxyl radical scavengers, but could be protected by singlet oxygen scavengers, suggesting that either singlet oxygen or a singlet oxygen-like entity, possibly a copper-peroxide complex, but not free hydroxyl radical probably plays a role in the DNA damage. The above results would suggest that macromolecule-associated copper and reactive oxygen generation may be important factors in the mechanism of 1,4-HQ and other phenolic compound- induced DNA damage in target cells.

L4 ANSWER 4 OF 26 CANCERLIT

AN 94185039 CANCERLIT

DN 94185039 PubMed ID: 8137307

TI Reactive oxygen-dependent DNA damage resulting from the oxidation of phenolic compounds by a copper-redox cycle mechanism.

AU Li Y; Trush M A

CS Department of Environmental Health Sciences, Johns Hopkins University
School of Hygiene and Public Health, Baltimore, Maryland 21205.

NC ES03760 (NIEHS)

ES03819 (NIEHS)

ES05131 (NIEHS)

+

SO CANCER RESEARCH, (1994 Apr 1) 54 (7 Suppl) 1895s-1898s.

Journal code: 2984705R. ISSN: 0008-5472.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS MEDLINE; Priority Journals

OS MEDLINE 94185039

EM 199404

ED Entered STN: 19941107

Last Updated on STN: 19970509

AB Recently, copper has been shown to be capable of mediating the activation of several xenobiotics producing reactive oxygen and other radicals. Since copper exists in the nucleus and is closely associated with chromosomes and DNA bases, in this study we have investigated whether the activation

of 1,4-hydroquinone (1,4-HQ) and a variety of other phenolic compounds by copper can induce strand breaks in double-stranded phi X-174 RF I DNA (phi X-174 relaxed form I DNA). In the presence of micromolar concentrations of Cu(II), DNA strand breaks were induced by 1,4-HQ and other phenolic compounds including 4,4'-biphenol, catechol, 1,2,4-benzenetriol, 2-methoxyestradiol, 2-hydroxyestradiol, diethylstilbestrol, butylated hydroxytoluene, butylated hydroxyanisole, tert-butylhydroquinone, ferulic acid, caffeic acid, chlorogenic acid, eugenol, 2-acetamidophenol, and acetaminophen. Structure-activity analysis shows that in the presence of Cu(II), the DNA cleaving activity for phenolic compounds with a 1,4-hydroquinone structure, such as 1,2,4-benzenetriol and tert-butylhydroquinone is greater than those with a catechol group (catechol, 2-hydroxyestradiol and caffeic acid). Those compounds having one phenol group, such as eugenol, 2-acetamidophenol, and acetaminophen, are the least reactive. In addition, the induced DNA strand breaks could be inhibited by bathocuproinedisulfonic acid, a Cu(I)-specific chelator, or catalase indicating that a Cu(II)/Cu(I) redox cycle and H2O2 generation are two major determinants involved in the observed DNA damage. Using reactive oxygen scavengers, it was observed that the DNA strand breaks induced by the 1,4-HQ/Cu(II) system could not be efficiently inhibited by hydroxyl radical scavengers, but could be protected by singlet oxygen scavengers, suggesting that either singlet oxygen or a singlet oxygen-like entity, possibly a copper-peroxide complex, but not free hydroxyl radical probably plays a role in the DNA damage. The above results would suggest that macromolecule-associated copper and reactive oxygen generation may be important factors in the mechanism of 1,4-HQ and other phenolic compound-induced DNA damage in target cells.

L4 ANSWER 5 OF 26 CAPLUS COPYRIGHT 2002 ACS
 AN 2002:575756 CAPLUS
 DN 137:103879
 TI Use of **eugenol**, alone and in combination with 2-
methoxyestradiol, as prophylaxis for cancers
 IN Slaga, Thomas J.; Kumar, Addanki P.; Alworth, William
 PA USA
 SO U.S. Pat. Appl. Publ., 9 pp., Cont.-in-part of U. S. Ser. No. 527,283,
 abandoned.
 CODEN: USXXCO
 DT Patent
 LA English
 FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002103174	A1	20020801	US 2001-4105	20011204
	US 2002068724	A1	20020606	US 2001-777151	20010205
PRAI	US 2000-527283	B2	20000317		
	US 2001-777151	A2	20010205		
	US 2001-777559	B2	20010206		

AB The invention discloses the use of **eugenol**, alone and in combination with 2-**methoxyestradiol** in the context of prostate cancer prophylaxis and treatment, and in the treatment and prevention of noncancerous enlargement of prostate glands.

L4 ANSWER 6 OF 26 CAPLUS COPYRIGHT 2002 ACS
 AN 2002:221214 CAPLUS
 DN 136:241655
 TI Estradiol derivatives as agents and methods for the prevention of initial onset and recurrence of existing cancers
 IN Slaga, Thomas J.; Kumar, Addanki P.; Alworth, William
 PA Oncology Sciences Corporation, USA
 SO U.S. Pat. Appl. Publ., 12 pp., Cont.-in-part of U.S. Ser. No. 527,283,
 abandoned.
 CODEN: USXXCO
 DT Patent
 LA English
 FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002035098	A1	20020321	US 2001-808408	20010314
	WO 2002072021	A2	20020919	WO 2002-US7445	20020313
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRAI	US 2000-527283	B2	20000317		
	US 2001-808408	A1	20010314		
AB	The use of 2-methoxyestradiol, analogs of 2-methoxyestradiol, their method of synthesis and therapeutic use, and the use of combinations of 2-methoxyestradiol and its analogs with synergistic compds. (namely eugenol), all in the prevention of initial onset cancers and the recurrence of previously existing cancers is described.				
L4	ANSWER 7 OF 26 CAPLUS COPYRIGHT 2002 ACS				
AN	2002:51983 CAPLUS				
DN	136:79754				
TI	Use of eugenol, alone, and in combination with other chemopreventative agents as prophylaxis for cancers				
IN	Slaga, Thomas J.; Kumar, Addanki P.; Alworth, William				
PA	Biochemix, Inc., USA				
SO	U.S. Pat. Appl. Publ., 5 pp., Cont.-in-part of U. S. Ser. No. 527,283, abandoned.				
	CODEN: USXXCO				
DT	Patent				
LA	English				
FAN.CNT	4				
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002006918	A1	20020117	US 2001-780269	20010209
	WO 2002062348	A1	20020815	WO 2002-US2826	20020201
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	WO 2002062347	A1	20020815	WO 2002-US2827	20020201
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	WO 2002062349	A1	20020815	WO 2002-US2828	20020201
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRAI	US 2000-527283	B2	20000317		
	US 2001-777151	A1	20010205		
	US 2001-777559	A1	20010206		

US 2001-780269 A1 20010209

AB The use of **eugenol**, alone and in combination with 2-**methoxyestradiol** (2-ME) in the context of prostate cancer prophylaxis and treatment.

L4 ANSWER 8 OF 26 CAPLUS COPYRIGHT 2002 ACS

AN 1994:238022 CAPLUS

DN 120:238022

TI Reactive oxygen-dependent DNA damage resulting from the oxidation of phenolic compounds by a copper-redox cycle mechanism

AU Li, Yunbo; Tursh, Michael A.

CS Sch. Hyg. Public Health, Johns Hopkins Univ., Baltimore, MD, 21205, USA

SO Cancer Research (1994), 54(7, Suppl.), 1895s-1898s

CODEN: CNREA8; ISSN: 0008-5472

DT Journal

LA English

AB Recently, copper has been shown to be capable of mediating the activation of several xenobiotics producing reactive oxygen and other radicals. Since copper exists in the nucleus and is closely assocd. with chromosomes and DNA bases, in this study the authors have investigated whether the activation of 1,4-hydroquinone (1,4-HQ) and a variety of other phenolic compds. by copper can induce strand breaks in double-stranded .phi.X-174 RF I DNA (.phi.X-174 relaxed form I DNA). In the presence of micromolar concns. of Cu(II), DNA strand breaks were induced by 1,4-HQ and other phenolic compds. including 4,4'-biphenol, catechol, 1,2,4-benzenetriol, 2-**methoxyestradiol**, 2-hydroxyestradiol, diethylstilbestrol, butylated hydroxytoluene, butylated hydroxyanisole, tert-butylhydroquinone, ferulic acid, caffeic acid, chlorogenic acid, **eugenol**, 2-acetamidophenol, and acetaminophen. Structure-activity anal. shows that in the presence of Cu(II), the DNA cleaving activity for phenolic compds. with a 1,4-hydroquinone structure, such as 1,2,4-benzenetriol and tert-butylhydroquinone is greater than those with a catechol group (catechol, 2-hydroxyestradiol and caffeic acid). Those compds. having one phenol group, such as **eugenol**, 2-acetamidophenol, and acetaminophen, are the least reactive. In addn., the induced DNA strand breaks could be inhibited by bathocuproinedisulfonic acid, a Cu(I)-specific chelator, or catalase indicating that a Cu(II)/Cu(I) redox cycle and H2O2 generation are two major determinants involved in the obsd. DNA damage. Using reactive oxygen scavengers, it was obsd. that the DNA strand breaks induced by the 1,4-HQ/Cu(II) system could not be efficiently inhibited by hydroxyl radical scavengers, but could be protected by singlet oxygen scavengers, suggesting that either singlet oxygen or a singlet oxygen-like entity, possibly a copper-peroxide complex, but not free hydroxyl radical probably plays a role in the DNA damage. The above results would suggest that macromol.-assocd. copper and reactive oxygen generation may be important factors in the mechanism of 1,4-HQ and other phenolic compd.-induced DNA damage in target cells.

L4 ANSWER 9 OF 26 DRUGU COPYRIGHT 2002 THOMSON DERWENT

AN 2001-47952 DRUGU P

TI Development of novel apoptotic inducers for prostate cancer therapy.

AU Kumar A P; Garcia G E; Rajnarayanan R; Alworth W L; Slaga T J

CS AMC-Cancer-Res.Cent.; Univ.Tulane

LO Denver, Colo.; New Orleans, La., USA

SO Proc.Am.Assoc.Cancer Res. (42, 92 Meet., 448, 2001) 1 Ref.

ISSN:

0197-016X

AV AMC Cancer Research Center, Denver, CO, U.S.A.

LA English

DT Journal

FA AB; LA; CT

FS Literature

AN 2001-47952 DRUGU P

AB This study elucidated 2-**methoxyestradiol**'s (2-ME) critical moiety for tumor growth inhibition. The effect of 16-epiestriol, **Eugenol** (4-allyl-2-methoxyphenol), curcumin, 4-methoxyphenol (mequinol) in inhibiting human prostate cancer cell growth was studied.

16-Epiestriol had no growth inhibitory activity indicating that the methoxy group was critical for its growth inhibitory activity. Conversely **eugenol** inhibited the growth of prostate cancer cells indicating those structures simpler than the steroidal nucleus can also be developed as therapeutics for prostate cancer. The IC50s for curcumin and 4-methoxyphenol was much higher than 2-ME and **eugenol**. (conference abstract: 92nd Annual Meeting of the American Association for Cancer Research, New Orleans, Louisiana, USA, 2001). (No EX).

ABEX (E124)

L4 ANSWER 10 OF 26 DRUGU COPYRIGHT 2002 THOMSON DERWENT
AN 1994-25367 DRUGU P B E S
TI Reactive oxygen-dependent DNA damage resulting from the oxidation of phenolic compounds by a copper-redox cycle mechanism.
AU Li Y; Trush M A
CS Univ. Johns-Hopkins
LO Baltimore, Maryland, United States
SO Cancer Res. (54, No. 7, Suppl., 1895s-1898s, 19 1 Fig. 2 Tab. 31 Ref. CODEN: CNREA8 ISSN: 0008-5472
AV Department of Environmental Health Sciences, Room 7032, The Johns Hopkins School of Hygiene and Public Health, 615 N. Wolfe Street, Baltimore, MD 21205, U.S.A. (M.A.T.).

LA English
DT Journal

FA AB; LA; CT; MPC

FS Literature

AN 1994-25367 DRUGU P B E S

AB With uM levels of cupric sulfate (Fisher-Sci.), DNA strand breaks were induced by 1,4-hydroquinone (HQ), 4,4'-biphenol, catechol (all Sigma-Chem.), 1,2,4-benzenetriol (Aldrich), 2-methoxyestradiol (Sigma-Chem.), hydroxyestradiol (Steraloids), diethylstilbestrol, butylated-hydroxytoluene (BHT), butylated-hydroxyanisole (BHA), tert-butylhydroquinone (BHQ, all Sigma-Chem.), ferulate, caffeate, chlorogenate (all Aldrich), **eugenol**, paracetamol and acetaminodophenol-2 (all Sigma-Chem.). The induced strand breaks were inhibited by bathocuproinedisulfonate (BCS). The DNA cleaving activity for compounds with a 1,4-hydroquinone structure was greater than those with a catechol group. Benzo(a)pyrene, estradiol (E2, Sigma-Chem.) and 4-hydroxy-E2 (steraloids) caused no DNA damage.

ABEX In the presence of 10 uM Cu(II), 10 uM HQ induced extensive DNA strand breaks; this effect was inhibited by BCS (40 uM). Catalase, but not Cu, Zn superoxide dismutase, inhibited the HQ/Cu(II)-induced DNA strand breaks; anaerobic conditions were also protective. Among mannitol, N-tert-butyl alpha-phenylnitrone, Na azide and 2,2,6,6-tetramethyl 4-piperidone, the hydroxyl radical scavengers did not prevent the HQ/Cu(II)-induced DNA strand breaks, whereas the single oxygen scavengers had some inhibitory effect. 1,2,4-benzenetriol was more effective than phenol, 4,4'-biphenol and catechol at causing DNA strand breaks in the presence of Cu(II). 2-Hydroxyestradiol/Cu(II) caused extensive DNA strand breaks as well as significant O2 consumption and H2O2 generation. 2-Methoxyestradiol/Cu(II) only induced slight DNA strand breaks, and 4-hydroxyestradiol/Cu(II) showed no DNA cleaving activity. Diethylstilbestrol/Cu(II) was only slight effective. In the presence of Cu(II), BHQ induced extensive DNA degradation, while BHA and BHT were less potent. Caffeate/Cu(II) showed a stronger DNA cleaving capability than did ferulate. In the presence of Cu(II), chlorogenate, **eugenol**, 2-acetamidophenol and paracetamol induced only slight DNA strand breaks, while benzo(a)pyrene did not damage. (E61/MB)

L4 ANSWER 11 OF 26 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

AN 94133041 EMBASE

DN 1994133041

TI Reactive oxygen-dependent DNA damage resulting from the oxidation of phenolic compounds by a copper-redox cycle mechanism.

AU Li Y.; Trush M.A.

CS Environmental Health Sciences Dept., J. Hopkins Hygiene/Public Hlth. Sch.,

SO 615 N. Wolfe Street, Baltimore, MD 21205, United States
Cancer Research, (1994) 54/7 SUPPL. (1895s-1898s).
ISSN: 0008-5472 CODEN: CNREA8
CY United States
DT Journal; Conference Article
FS 016 Cancer
LA English
SL English
AB

Recently, copper has been shown to be capable of mediating the activation of several xenobiotics producing reactive oxygen and other radicals. Since copper exists in the nucleus and is closely associated with chromosomes and DNA bases, in this study we have investigated whether the activation of 1,4- hydroquinone (1,4-HQ) and a variety of other phenolic compounds by copper can induce strand breaks in double-stranded .phi.X-174 RF I DNA (.phi.X-174 relaxed form I DNA). In the presence of micromolar concentrations of Cu(II), DNA strand breaks were induced by 1,4-HQ and other phenolic compounds including 4,4'-biphenol, catechol, 1,2,4-benzenetriol, 2-methoxyestradiol, 2- hydroxyestradiol, diethylstilbestrol, butylated hydroxytoluene, butylated hydroxyanisole, tert-butylhydroquinone, ferulic acid, caffeic acid, chlorogenic acid, **eugenol**, 2-acetamidophenol, and acetaminophen. Structure- activity analysis shows that in the presence of Cu(II), the DNA cleaving activity for phenolic compounds with a 1,4-hydroquinone structure, such as 1,2,4-benzenetriol and tert-butylhydroquinone is greater than those with a catechol group (catechol, 2-hydroxyestradiol and caffeic acid). Those compounds having one phenol group, such as **eugenol**, 2-acetamidophenol, and acetaminophen, are the least reactive. In addition, the induced DNA strand breaks could be inhibited by bathocuproinedisulfonic acid, a Cu(I)-specific chelator, or catalase indicating that a Cu(II)/Cu(I) redox cycle and H2O2 generation are two major determinants involved in the observed DNA damage. Using reactive oxygen scavengers, it was observed that the DNA strand breaks induced by the 1,4-HQ/Cu(II) system could not be efficiently inhibited by hydroxyl radical scavengers, but could be protected by singlet oxygen scavengers, suggesting that either singlet oxygen or a singlet oxygen-like entity, possibly a copper-peroxide complex, but not free hydroxyl radical probably plays a role in the DNA damage. The above results would suggest that macromolecule-associated copper and reactive oxygen generation may be important factors in the mechanism of 1,4-HQ and other phenolic compound-induced DNA damage in target cells.

L4 ANSWER 12 OF 26 IFIPAT COPYRIGHT 2002 IFI
AN 10159532 IFIPAT;IFIUDB;IFICDB
TI USE OF **EUGENOL**, ALONE, AND IN COMBINATION WITH OTHER
CHEMOPREVENTATIVE AGENTS AS PROPHYLAXIS FOR CANCERS
INF Alworth; William, New Orleans, LA, US
Kumar; Addanki P., Denver, CO, US
Slaga; Thomas J., Golden, CO, US
IN Alworth William; Kumar Addanki P; Slaga Thomas J
PAF Unassigned
PA Unassigned Or Assigned To Individual (68000)
AG DAVID G. HENRY, 900 Washington Avenue, P.O. Box 1470, Waco, TX, 76701, US
PI US 2002103174 A1 20020801
AI US 2001-4105 20011204
RLI US 2000-527283 20000317 CONTINUATION-IN-PART ABANDONED
US 2001-777151 20010205 CONTINUATION-IN-PART PENDING
US 2001-777559 20010206 CONTINUATION-IN-PART ABANDONED
FI US 2002103174 20020801
DT Utility; Patent Application - First Publication
FS CHEMICAL
FS APPLICATION
CLMN 9
AB The use of **eugenol**, alone and in combination with
2methoxyestradiol (2-ME) in the context of prostate cancer prophylaxes
and treatment, and in the treatment and prevention of non-cancerous
enlargement of prostate glands.
CLMN 9

L4 ANSWER 13 OF 26 IFIPAT COPYRIGHT 2002 IFI
 AN 10091534 IFIPAT;IFIUDB;IFICDB
 TI AGENTS AND METHODS FOR THE PREVENTION OF INITIAL ONSET AND RECURRENCE OF EXISTING CANCERS
 INF Alworth; William, New Orleans, LA, US
 Kumar; Addanki P., Denver, CO, US
 Slaga; Thomas J., Denver, CO, US
 IN Alworth William; Kumar Addanki P; Slaga Thomas J
 PAF Oncology Sciences Corporation, Austin, TX, US
 PA Oncology Sciences Corp
 AG DAVID G. HENRY, 900 Washington Avenue, P.O. Box 1470, Waco, TX, 76701, US
 PI US 2002035098 A1 20020321
 AI US 2001-808408 20010314
 RLI US 2000-527283 20000317 CONTINUATION-IN-PART ABANDONED
 FI US 2002035098 20020321
 DT Utility; Patent Application - First Publication
 FS CHEMICAL
 FS APPLICATION
 CLMN 15
 AB The use of 2-**methoxyestradiol**, analogues of 2-**methoxyestradiol**, their method of synthesis and therapeutic use, and the use of combinations of the 2 **methoxyestradiol** and its analogues with synergistic compounds (namely **eugenol**), all in the prevention of initial onset cancers and the recurrence of previously existing cancers.

CLMN 15

L4 ANSWER 14 OF 26 IFIPAT COPYRIGHT 2002 IFI
 AN 10063396 IFIPAT;IFIUDB;IFICDB
 TI USE OF **EUGENOL**, ALONE, AND IN COMBINATION WITH OTHER CHEMOPREVENTATIVE AGENTS AS PROPHYLAXIS FOR CANCERS; PROSTATE CANCER
 INF Alworth; William, New Orleans, LA, US
 Kumar; Addanki P., Denver, CO, US
 Slaga; Thomas J., Austin, TX, US
 IN Alworth William; Kumar Addanki P; Slaga Thomas J
 PAF Biochemix, Inc., Austin, TX, US
 PA Biochemix Inc
 AG DAVID G. HENRY, 900 Washington Avenue, P.O. Box 1470, Waco, TX, 76701, US
 PI US 2002006918 A1 20020117
 AI US 2001-780269 20010209
 RLI US 2000-527283 20000317 CONTINUATION-IN-PART ABANDONED
 FI US 2002006918 20020117
 DT Utility; Patent Application - First Publication
 FS CHEMICAL
 FS APPLICATION
 CLMN 5
 AB The use of **eugenol**, alone and in combination with 2methoxyestradiol (2-ME) in the context of prostate cancer prophylaxes and treatment.

CLMN 5

L4 ANSWER 15 OF 26 LIFESCI COPYRIGHT 2002 CSA
 AN 95:3046 LIFESCI
 TI Reactive oxygen-dependent DNA damage resulting from the oxidation of phenolic compounds by a copper-redox cycle mechanism
 AU Li, Yunbo; Trush, M.A.*
 CS Dep. Environ. Health Sci., Rm. 7032, Johns Hopkins Sch. Hyg. and Pub. Health, 615 N. Wolfe St., Baltimore, MD 21205, USA
 SO CANCER RES., (1994) vol. 54, no. 7 suppl., pp. 1895S-1899S.
 ISSN: 0008-5472.
 DT Journal
 FS N
 LA English
 SL English
 AB Recently, copper has been shown to be capable of mediating the activation of several xenobiotics producing reactive oxygen and other radicals. Since

copper exists in the nucleus and is closely associated with chromosomes and DNA bases, we have investigated whether the activation of 1,4-hydroquinone (1,4-HQ) and a variety of other phenolic compounds by copper can induce strand breaks in double-stranded Phi X-174 RF I DNA (Phi X-174 relaxed form I DNA). In the presence of micromolar concentrations of Cu(II), DNA strand breaks were induced by 1,4-HQ and other phenolic compounds including 4,4'-biphenol, catechol, 1,2,4-benzenetriol, 2-methoxyestradiol, 2-hydroxyestradiol, diethylstilbestrol, butylated hydroxytoluene, butylated hydroxyanisole, tert-butylhydroquinone, ferulic acid, caffeic acid, chlorogenic acid, eugenol, 2-acetamidophenol, and acetaminophen. Structure-activity analysis shows that in the presence of Cu(II), the DNA cleaving activity for phenolic compounds with a 1,4-hydroquinone structure, such as 1,2,4-benzenetriol and tert-butylhydroquinone is greater than those with a catechol group (catechol, 2-hydroxyestradiol and caffeic acid). Those compounds having one phenol group, such as eugenol, 2-acetamidophenol, and acetaminophen, are the least reactive. In addition, the induced DNA strand breaks could be inhibited by bathocuproinedisulfonic acid, a Cu(I)-specific chelator, or catalase indicating that a Cu(II)/Cu(I) redox cycle and H sub(2)O sub(2) generation are two major determinants involved in the observed DNA damage. Using reactive oxygen scavengers, it was observed that the DNA strand breaks induced by the 1,4-HQ/Cu(II) system could not be efficiently inhibited by hydroxyl radical scavengers, but could be protected by singlet oxygen scavengers, suggesting that either singlet oxygen or a singlet oxygen-like entity, possibly a copper-peroxide complex, but not free hydroxyl radical probably plays a role in the DNA damage. The above results would suggest that macromolecule-associated copper and reactive oxygen generation may be important factors in the mechanism of 1,4-HQ and other phenolic compound-induced DNA damage in target cells.

L4 ANSWER 16 OF 26 MEDLINE

AN 94185039 MEDLINE

DN 94185039 PubMed ID: 8137307

TI Reactive oxygen-dependent DNA damage resulting from the oxidation of phenolic compounds by a copper-redox cycle mechanism.

AU Li Y; Trush M A

CS Department of Environmental Health Sciences, Johns Hopkins University School of Hygiene and Public Health, Baltimore, Maryland 21205.

NC ES03760 (NIEHS)

ES03819 (NIEHS)

ES05131 (NIEHS)

+

SO CANCER RESEARCH, (1994 Apr 1) 54 (7 Suppl) 1895s-1898s.

Journal code: 2984705R. ISSN: 0008-5472.

CY United States

DT Journal; Article, (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199404

ED Entered STN: 19940509

Last Updated on STN: 19970203

Entered Medline: 19940425

AB Recently, copper has been shown to be capable of mediating the activation of several xenobiotics producing reactive oxygen and other radicals. Since copper exists in the nucleus and is closely associated with chromosomes and DNA bases, in this study we have investigated whether the activation of 1,4-hydroquinone (1,4-HQ) and a variety of other phenolic compounds by copper can induce strand breaks in double-stranded phi X-174 RF I DNA (phi X-174 relaxed form I DNA). In the presence of micromolar concentrations of Cu(II), DNA strand breaks were induced by 1,4-HQ and other phenolic compounds including 4,4'-biphenol, catechol, 1,2,4-benzenetriol, 2-methoxyestradiol, 2-hydroxyestradiol, diethylstilbestrol, butylated hydroxytoluene, butylated hydroxyanisole, tert-butylhydroquinone, ferulic acid, caffeic acid, chlorogenic acid, eugenol, 2-acetamidophenol, and acetaminophen. Structure-activity analysis shows that in the presence of Cu(II), the DNA cleaving activity

for phenolic compounds with a 1,4-hydroquinone structure, such as 1,2,4-benzenetriol and tert-butylhydroquinone is greater than those with a catechol group (catechol, 2-hydroxyestradiol and caffeic acid). Those compounds having one phenol group, such as **eugenol**, 2-acetamidophenol, and acetaminophen, are the least reactive. In addition, the induced DNA strand breaks could be inhibited by bathocuproinedisulfonic acid, a Cu(I)-specific chelator, or catalase indicating that a Cu(II)/Cu(I) redox cycle and H₂O₂ generation are two major determinants involved in the observed DNA damage. Using reactive oxygen scavengers, it was observed that the DNA strand breaks induced by the 1,4-HQ/Cu(II) system could not be efficiently inhibited by hydroxyl radical scavengers, but could be protected by singlet oxygen scavengers, suggesting that either singlet oxygen or a singlet oxygen-like entity, possibly a copper-peroxide complex, but not free hydroxyl radical probably plays a role in the DNA damage. The above results would suggest that macromolecule-associated copper and reactive oxygen generation may be important factors in the mechanism of 1,4-HQ and other phenolic compound-induced DNA damage in target cells.

L4 ANSWER 17 OF 26 SCISEARCH COPYRIGHT 2002 ISI (R)

AN 94:195003 SCISEARCH

GA The Genuine Article (R) Number: NE168

TI REACTIVE OXYGEN-DEPENDENT DNA-DAMAGE RESULTING FROM THE OXIDATION OF PHENOLIC-COMPOUNDS BY A COPPER-REDOX CYCLE MECHANISM

AU LI Y B (Reprint); TRUSH M A

CS JOHNS HOPKINS UNIV, SCH HYG & PUBL HLTH, DEPT ENVIRONM HLTH SCI, DIV TOXICOL SCI, ROOM 7032, BALTIMORE, MD, 21205 (Reprint)

CYA USA

SO CANCER RESEARCH, (01 APR 1994) Vol. 54, No. 7, Supp. S, pp. S1895-S1898. ISSN: 0008-5472.

DT Article; Journal

FS LIFE; CLIN

LA ENGLISH

REC Reference Count: 31

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Recently, copper has been shown to be capable of mediating the activation of several xenobiotics producing reactive oxygen and other radicals. Since copper exists in the nucleus and is closely associated with chromosomes and DNA bases, in this study we have investigated whether the activation of 1,4-hydroquinone (1,4-HQ) and a variety of other phenolic compounds by copper can induce strand breaks in double-stranded phiX-174 RF I DNA (phiX-174 relaxed form I DNA). In the presence of micromolar concentrations of Cu(II), DNA strand breaks were induced by 1,4-HQ and other phenolic compounds including 4,4'-biphenol, catechol, 1,2,4-benzenetriol, 2-methoxyestradiol, 2-hydroxyestradiol, diethylstilbestrol, butylated hydroxytoluene, butylated hydroxyanisole, tert-butylhydroquinone, ferulic acid, caffeic acid, chlorogenic acid, **eugenol**, 2-acetamidophenol, and acetaminophen. Structure-activity analysis shows that in the presence of Cu(II), the DNA cleaving activity for phenolic compounds with a 1,4-hydroquinone structure, such as 1,2,4-benzenetriol and tert-butylhydroquinone is greater than those with a catechol group (catechol, 2-hydroxyestradiol and caffeic acid). Those compounds having one phenol group, such as **eugenol**, 2-acetamidophenol, and acetaminophen, are the least reactive. In addition, the induced DNA strand breaks could be inhibited by bathocuproinedisulfonic acid, a Cu(I)-specific chelator, or catalase indicating that a Cu(II)/Cu(I) redox cycle and H₂O₂ generation are two major determinants involved in the observed DNA damage. Using reactive oxygen scavengers, it was observed that the DNA strand breaks induced by the 1,4-HQ/Cu(II) system could not be efficiently inhibited by hydroxyl radical scavengers, but could be protected by singlet oxygen scavengers, suggesting that either singlet oxygen or a singlet oxygen-like entity, possibly a copper-peroxide complex, but not free hydroxyl radical probably plays a role in the DNA damage. The above results would suggest that macromolecule-associated copper and reactive oxygen generation may be important factors in the mechanism of 1,4-HQ and other phenolic compound-induced DNA damage in target cells.

L4 ANSWER 18 OF 26 TOXCENTER COPYRIGHT 2002 ACS
 AN 2002:182446 TOXCENTER
 CP Copyright 2002 ACS
 DN CA13708103879V
 TI Use of **eugenol**, alone and in combination with 2-
methoxyestradiol, as prophylaxis for cancers
 AU Slaga, Thomas J.; Kumar, Addanki P.; Alworth, William
 PI US 2002103174 A1 1 Aug 2002
 SO (2002) U.S. Pat. Appl. Publ., 9 pp., Cont.-in-part of U. S. Ser. No.
 527,283, abandoned.
 CODEN: USXXCO.
 CY UNITED STATES
 DT Patent
 FS CAPLUS
 OS CAPLUS 2002:575756
 LA English
 ED Entered STN: 20020820
 Last Updated on STN: 20020820
 AB The invention discloses the use of **eugenol**, alone and in
 combination with 2-**methoxyestradiol** in the context of prostate
 cancer prophylaxis and treatment, and in the treatment and prevention of
 noncancerous enlargement of prostate glands.

L4 ANSWER 19 OF 26 TOXCENTER COPYRIGHT 2002 ACS
 AN 2002:84120 TOXCENTER
 CP Copyright 2002 ACS
 DN CA13616241655Z
 TI Estradiol derivatives as agents and methods for the prevention of initial
 onset and recurrence of existing cancers
 AU Slaga, Thomas J.; Kumar, Addanki P.; Alworth, William
 CS ASSIGNEE: Oncology Sciences Corporation
 PI US 2002035098 A1 21 Mar 2002
 SO (2002) U.S. Pat. Appl. Publ., 12 pp., Cont.-in-part of U.S. Ser. No.
 527,283, abandoned.
 CODEN: USXXCO.
 CY UNITED STATES
 DT Patent
 FS CAPLUS
 OS CAPLUS 2002:221214
 LA English
 ED Entered STN: 20020409
 Last Updated on STN: 20020423
 AB The use of 2-**methoxyestradiol**, analogs of 2-
methoxyestradiol, their method of synthesis and therapeutic use,
 and the use of combinations of 2-**methoxyestradiol** and its
 analogs with synergistic compds. (namely **eugenol**), all in the
 prevention of initial onset cancers and the recurrence of previously
 existing cancers is described.

L4 ANSWER 20 OF 26 TOXCENTER COPYRIGHT 2002 ACS
 AN 2002:36024 TOXCENTER
 CP Copyright 2002 ACS
 DN CA13606079754G
 TI Use of **eugenol**, alone, and in combination with other
 chemopreventative agents as prophylaxis for cancers
 AU Slaga, Thomas J.; Kumar, Addanki P.; Alworth, William
 CS ASSIGNEE: Biochemix, Inc.
 PI US 2002006918 A1 17 Jan 2002
 SO (2002) U.S. Pat. Appl. Publ., 5 pp., Cont.-in-part of U. S. Ser. No.
 527,283, abandoned.
 CODEN: USXXCO.
 CY UNITED STATES
 DT Patent
 FS CAPLUS
 OS CAPLUS 2002:51983
 LA English

ED Entered STN: 20020205
Last Updated on STN: 20020423
AB The use of **eugenol**, alone and in combination with 2-**methoxyestradiol** (2-ME) in the context of prostate cancer prophylaxis and treatment.

L4 ANSWER 21 OF 26 TOXCENTER COPYRIGHT 2002 ACS
AN 1994:140310 TOXCENTER
CP Copyright 2002 ACS
DN CA12019238022E

TI Reactive oxygen-dependent DNA damage resulting from the oxidation of phenolic compounds by a copper-redox cycle mechanism
AU Li, Yunbo; Tursh, Michael A.
CS Sch. Hyg. Public Health, Johns Hopkins Univ., Baltimore, MD, 21205, USA.
SO Cancer Research, (1994) Vol. 54, No. 7, Suppl., pp. 1895s-1898s.
CODEN: CNREA8. ISSN: 0008-5472.

CY UNITED STATES

DT Journal

FS CAPLUS

OS CAPLUS 1994:238022

LA English

ED Entered STN: 20011116

Last Updated on STN: 20020917

AB Recently, copper has been shown to be capable of mediating the activation of several xenobiotics producing reactive oxygen and other radicals. Since copper exists in the nucleus and is closely assocd. with chromosomes and DNA bases, in this study the authors have investigated whether the activation of 1,4-hydroquinone (1,4-HQ) and a variety of other phenolic compds. by copper can induce strand breaks in double-stranded .phi.X-174 RF I DNA (.phi.X-174 relaxed form I DNA). In the presence of micromolar concns. of Cu(II), DNA strand breaks were induced by 1,4-HQ and other phenolic compds. including 4,4'-biphenol, catechol, 1,2,4-benzenetriol, 2-**methoxyestradiol**, 2-hydroxyestradiol, diethylstilbestrol, butylated hydroxytoluene, butylated hydroxyanisole, tert-butylhydroquinone, ferulic acid, caffeic acid, chlorogenic acid, **eugenol**, 2-acetamidophenol, and acetaminophen. Structure-activity anal. shows that in the presence of Cu(II), the DNA cleaving activity for phenolic compds. with a 1,4-hydroquinone structure, such as 1,2,4-benzenetriol and tert-butylhydroquinone is greater than those with a catechol group (catechol, 2-hydroxyestradiol and caffeic acid). Those compds. having one phenol group, such as **eugenol**, 2-acetamidophenol, and acetaminophen, are the least reactive. In addn., the induced DNA strand breaks could be inhibited by bathocuproinedisulfonic acid, a Cu(I)-specific chelator, or catalase indicating that a Cu(II)/Cu(I) redox cycle and H2O2 generation are two major determinants involved in the obsd. DNA damage. Using reactive oxygen scavengers, it was obsd. that the DNA strand breaks induced by the 1,4-HQ/Cu(II) system could not be efficiently inhibited by hydroxyl radical scavengers, but could be protected by singlet oxygen scavengers, suggesting that either singlet oxygen or a singlet oxygen-like entity, possibly a copper-peroxide complex, but not free hydroxyl radical probably plays a role in the DNA damage. The above results would suggest that macromol.-assocd. copper and reactive oxygen generation may be important factors in the mechanism of 1,4-HQ and other phenolic compd.-induced DNA damage in target cells.

L4 ANSWER 22 OF 26 TOXCENTER COPYRIGHT 2002 ACS
AN 1994:81496 TOXCENTER
CP Copyright 2002 BIOSIS
DN PREV199497241282

TI Reactive oxygen-dependent DNA damage resulting from the oxidation of phenolic compounds by a copper-redox cycle mechanism
AU Li, Yunbo; Trush, Michael A. (1)
CS (1) Dep. Environ. Health Sci., Room 7032, Johns Hopkins Sch. Hygiene Public Health, 615 N. Wolfe St., Baltimore, MD 21205 USA
SO Cancer Research, (1994) Vol. 54, No. 7 SUPPL., pp. 1895S-1898S.
ISSN: 0008-5472.

DT Article
FS BIOSIS
OS BIOSIS 1994:228282
LA English
ED Entered STN: 20011116

Last Updated on STN: 20011116

AB Recently, copper has been shown to be capable of mediating the activation of several xenobiotics producing reactive oxygen and other radicals. Since copper exists in the nucleus and is closely associated with chromosomes and DNA bases, in this study we have investigated whether the activation of 1,4-hydroquinone (1,4-HQ) and a variety of other phenolic compounds by copper can induce strand breaks in double-stranded vphi-X-174 RF I DNA (vphi-X-174 relaxed form I DNA). In the presence of micromolar concentrations of Cu(II), DNA strand breaks were induced by 1,4-HQ and other phenolic compounds including 4,4'-biphenol, catechol, 1,2,4-benzenetriol, 2-methoxyestradiol, 2-hydroxyestradiol, diethylstilbestrol, butylated hydroxytoluene, butylated hydroxyanisole, tert-butylhydroquinone, ferulic acid, caffeic acid, chlorogenic acid, eugenol, 2-acetamidophenol, and acetaminophen. Structure-activity analysis shows that in the presence of Cu(II), the DNA cleaving activity for phenolic compounds with a 1,4-hydroquinone structure, such as 1,2,4-benzenetriol and tertbutylhydroquinone is greater than those with a catechol group (catechol, 2-hydroxyestradiol and caffeic acid). Those compounds having one phenol group, such as eugenol, 2-acetamidophenol, and acetaminophen, are the least reactive. In addition, the induced DNA strand breaks could be inhibited by bathocuproinedisulfonic acid, a Cu(I)-specific chelator, or catalase indicating that a Cu(II)/Cu(I) redox cycle and H-2O-2 generation are two major determinants involved in the observed DNA damage. Using reactive oxygen scavengers, it was observed that the DNA strand breaks induced by the 1,4-HQ/Cu(II) system could not be efficiently inhibited by hydroxyl radical scavengers, but could be protected by singlet oxygen scavengers, suggesting that either singlet oxygen or a singlet oxygen-like entity, possibly a copper-peroxide complex, but not free hydroxyl radical probably plays a role in the DNA damage. The above results would suggest that macromolecule-associated copper and reactive oxygen generation may be important factors in the mechanism of 1,4-HQ and other phenolic compound-induced DNA damage in target cells.

L4 ANSWER 23 OF 26 TOXCENTER COPYRIGHT 2002 ACS
AN 1994:31261 TOXCENTER

DN 94185039 PubMed ID: 8137307

TI Reactive oxygen-dependent DNA damage resulting from the oxidation of phenolic compounds by a copper-redox cycle mechanism

AU Li Y; Trush M A

CS Department of Environmental Health Sciences, Johns Hopkins University
School of Hygiene and Public Health, Baltimore, Maryland 21205

NC ES03760 (NIEHS)

ES03819 (NIEHS)

ES05131 (NIEHS)

+

SO CANCER RESEARCH, (1994 Apr 1) 54 (7 Suppl) 1895s-1898s.
Journal Code: 2984705R. ISSN: 0008-5472.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

FS MEDLINE

OS MEDLINE 94185039

LA English

ED Entered STN: 20011116

Last Updated on STN: 20011116

AB Recently, copper has been shown to be capable of mediating the activation of several xenobiotics producing reactive oxygen and other radicals. Since copper exists in the nucleus and is closely associated with chromosomes and DNA bases, in this study we have investigated whether the activation of 1,4-hydroquinone (1,4-HQ) and a variety of other phenolic compounds by copper can induce strand breaks in double-stranded phi X-174 RF I DNA (phi X-174 relaxed form I DNA). In the presence of micromolar

concentrations of Cu(II), DNA strand breaks were induced by 1,4-HQ and other phenolic compounds including 4,4'-biphenol, catechol, 1,2,4-benzenetriol, 2-methoxyestradiol, 2-hydroxyestradiol, diethylstilbestrol, butylated hydroxytoluene, butylated hydroxyanisole, tert-butylhydroquinone, ferulic acid, caffeic acid, chlorogenic acid, **eugenol**, 2-acetamidophenol, and acetaminophen. Structure-activity analysis shows that in the presence of Cu(II), the DNA cleaving activity for phenolic compounds with a 1,4-hydroquinone structure, such as 1,2,4-benzenetriol and tert-butylhydroquinone is greater than those with a catechol group (catechol, 2-hydroxyestradiol and caffeic acid). Those compounds having one phenol group, such as **eugenol**, 2-acetamidophenol, and acetaminophen, are the least reactive. In addition, the induced DNA strand breaks could be inhibited by bathocuproinedisulfonic acid, a Cu(I)-specific chelator, or catalase indicating that a Cu(II)/Cu(I) redox cycle and H₂O₂ generation are two major determinants involved in the observed DNA damage. Using reactive oxygen scavengers, it was observed that the DNA strand breaks induced by the 1,4-HQ/Cu(II) system could not be efficiently inhibited by hydroxyl radical scavengers, but could be protected by singlet oxygen scavengers, suggesting that either singlet oxygen or a singlet oxygen-like entity, possibly a copper-peroxide complex, but not free hydroxyl radical probably plays a role in the DNA damage. The above results would suggest that macromolecule-associated copper and reactive oxygen generation may be important factors in the mechanism of 1,4-HQ and other phenolic compound-induced DNA damage in target cells.

L4 ANSWER 24 OF 26 USPATFULL
AN 2002:192103 USPATFULL
TI Use of **eugenol**, alone, and in combination with other chemopreventative agents as prophylaxis for cancers
IN Slaga, Thomas J., Golden, CO, UNITED STATES
Kumar, Addanki P., Denver, CO, UNITED STATES
Alworth, William, New Orleans, LA, UNITED STATES
PI US 2002103174 A1 20020801
AI US 2001-4105 A1 20011204 (10)
RLI Continuation-in-part of Ser. No. US 2000-527283, filed on 17 Mar 2000, ABANDONED Continuation-in-part of Ser. No. US 2001-777151, filed on 5 Feb 2001, PENDING Continuation-in-part of Ser. No. US 2001-777559, filed on 6 Feb 2001, ABANDONED
DT Utility
FS APPLICATION
LREP DAVID G. HENRY, 900 Washington Avenue, P.O. Box 1470, Waco, TX, 76701
CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN 5 Drawing Page(s)
LN.CNT 287
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The use of **eugenol**, alone and in combination with 2-methoxyestradiol (2-ME) in the context of prostate cancer prophylaxes and treatment, and in the treatment and prevention of non-cancerous enlargement of prostate glands.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 25 OF 26 USPATFULL
AN 2002:61262 USPATFULL
TI Agents and methods for the prevention of initial onset and recurrence of existing cancers
IN Slaga, Thomas J., Denver, CO, UNITED STATES
Kumar, Addanki P., Denver, CO, UNITED STATES
Alworth, William, New Orleans, LA, UNITED STATES
PA Oncology Sciences Corporation, Austin, TX, UNITED STATES (U.S. corporation)
PI US 2002035098 A1 20020321
AI US 2001-808408 A1 20010314 (9)
RLI Continuation-in-part of Ser. No. US 2000-527283, filed on 17 Mar 2000, ABANDONED

DT Utility
FS APPLICATION
LREP DAVID G. HENRY, 900 Washington Avenue, P.O. Box 1470, Waco, TX, 76701
CLMN Number of Claims: 15
ECL Exemplary Claim: 1
DRWN 7 Drawing Page(s)
LN.CNT 417

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The use of 2-**methoxyestradiol**, analogues of 2-**methoxyestradiol**, their method of synthesis and therapeutic use, and the use of combinations of the 2 **methoxyestradiol** and its analogues with synergistic compounds (namely **eugenol**), all in the prevention of initial onset cancers and the recurrence of previously existing cancers.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 26 OF 26 USPATFULL
AN 2002:12537 USPATFULL
TI Use of **eugenol**, alone, and in combination with other chemopreventative agents as prophylaxis for cancers
IN Slaga, Thomas J., Austin, TX, UNITED STATES
Kumar, Addanki P., Denver, CO, UNITED STATES
Alworth, William, New Orleans, LA, UNITED STATES
PA Biochemix, Inc., Austin, TX, UNITED STATES (U.S. corporation)
PI US 2002006918 A1 20020117
AI US 2001-780269 A1 20010209 (9)
RLI Continuation-in-part of Ser. No. US 2000-527283, filed on 17 Mar 2000, ABANDONED

DT Utility
FS APPLICATION
LREP DAVID G. HENRY, 900 Washington Avenue, P.O. Box 1470, Waco, TX, 76701
CLMN Number of Claims: 5
ECL Exemplary Claim: 1
DRWN 2 Drawing Page(s)
LN.CNT 175

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The use of **eugenol**, alone and in combination with 2-**methoxyestradiol** (2-ME) in the context of prostate cancer prophylaxes and treatment.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=>

PI WO 9640150 A1 19 Dec 1996
SO (1996) PCT Int. Appl., 31 pp.
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FS CAPLUS
OS CAPLUS 1997:127459
LA English
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AB A method for treating and preventing **benign prostatic hyperplasia** (BPH) and prostatic carcinoma involves administering a therapeutically effective amt. of a compd. which binds to SHBG and antagonizes the SHBG-mediated effects of both estradiol and 5.alpha.-androstan-3.alpha.,17.beta.-diol by preventing the binding of estradiol and 5.alpha.-androstan-3.alpha.,17.beta.-diol. Also disclosed are the compds. which bind SHBG and prevent the binding of estradiol and 5.alpha.-androstan-3.alpha.,17.beta.-diol, as well as a method of finding compds. which bind to SHBG and prevent the binding of estradiol.

TI Treatment and prevention of prostatic disease, including prostate cancer and **benign prostatic hyperplasia**, with compounds binding to sex hormone-binding globulin (SHBG), and method for therapeutic compound identification

AB A method for treating and preventing **benign prostatic hyperplasia** (BPH) and prostatic carcinoma involves administering a therapeutically effective amt. of a compd. which binds to SHBG and antagonizes the. . .

ST Miscellaneous Descriptors
sex hormone binding globulin antagonist therapeutic; **benign prostatic hyperplasia** SHBG antagonist; prostate disease SHBG antagonist; cancer prostate SHBG antagonist

RN . . . (Flutamide)
19216-56-9 (Prazosin)
63590-64-7 (Terazosin)
74191-85-8 (Doxazosin)
90357-06-5 (Casodex)
106133-20-4 (Tamsulosin)
119169-78-7 (Epristeride)
521-17-5 (.DELTA.5-Androstene-3.beta.,17.beta.-diol)
6038-31-9 (5.beta.-Androstan-3.beta.,17.beta.-diol)
58-22-0 (Testosterone)
362-07-2 (**2-Methoxyestradiol**)
521-18-6 (Dihydrotestosterone)
60-92-4 (Cyclic AMP)
RN 1852-53-5; 81403-80-7; 98319-26-7; 158493-17-5; 166174-54-5; 166174-94-3;
186446-10-6; 1851-23-6; 571-20-0; 16895-59-3

The Genuine Article (R) Number: YN232

TI Sex hormone-binding globulin mediates prostate androgen receptor action
via a novel signaling pathway
AU Ding V D H (Reprint); Moller D E; Feeney W P; Didolkar V; Nakhla A M;
Rhodes L; Rosner W; Smith R G
CS MERCK & CO INC, MERCK SHARP & DOHME RES LABS RY80W243, DEPT MOL
ENDOCRINOL, POB 2000, RAHWAY, NJ 07065 (Reprint); MERCK & CO INC, MERCK
SHARP & DOHME RES LABS, DEPT BIOCHEM & PHYSIOL, DEPT LAB ANIM RESOURCES,
RAHWAY, NJ 07065; COLUMBIA UNIV, ST LUKES ROOSEVELT HOSP CTR, DEPT MED,
COLL PHYS & SURG, NEW YORK, NY 10019
CYA USA
SO ENDOCRINOLOGY, (JAN 1998) Vol. 139, No. 1, pp. 213-218.
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20814-4110.
ISSN: 0013-7227.
DT Article; Journal
FS LIFE
LA English
REC Reference Count: 49

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Estradiol (E-2) and 5 alpha-androstan-3 alpha,17 beta-diol (3
alpha-diol) have been implicated in prostate hyperplasia in man and dogs,
but neither of these steroids bind to androgen receptors (ARs). Recently,
we reported that E-2 and 3 alpha-diol stimulated generation of
intracellular cAMP via binding to a complex of sex hormone-binding
globulin (SHBG) and its receptor (R-SHBG) On prostate cells. We speculated
that this pathway, involving steroids normally found in the prostate, was
involved in the indirect activation of ARs. Using the dog as a model to
test this hypothesis in normal prostate, we investigated whether E-2, 3
alpha-diol, and SHBG stimulated the production of the androgen-responsive
protein, arginine esterase (AE), the canine equivalent of human
prostate-specific antigen. In cultured dog prostate tissue preincubated
with SHBG, E-2 and 3 alpha-diol stimulated AE activity. These effects were
blocked by hydroxyflutamide, an AR antagonist, and by 2-
methoxyestradiol, a competitive inhibitor of E-2 and 3 alpha-diol
binding to SHBG. In the absence of exogenous steroids and SHBG, AE also
was significantly increased by treatment with forskolin or
8-Bromaadenosine-cAMP. These observations support the hypothesis that in
normal prostate, E-2 and 3 alpha-diol can amplify or substitute for
androgens, with regard to activation of the AR via the R-SHBG by a signal
transduction pathway involving cAMP. Because both E-2 and 3 alpha-diol are
involved in the pathogenesis of **benign prostatic
hyperplasia** in dogs and implicated in **benign
prostatic hyperplasia** in man, antagonism of the
prostatic SHBG pathway may offer a novel and attractive therapeutic
target.

AB . . . with SHBG, E-2 and 3 alpha-diol stimulated AE activity. These
effects were blocked by hydroxyflutamide, an AR antagonist, and by
2-methoxyestradiol, a competitive inhibitor of E-2 and 3
alpha-diol binding to SHBG. In the absence of exogenous steroids and SHBG,
AE. . . R-SHBG by a signal transduction pathway involving cAMP. Because
both E-2 and 3 alpha-diol are involved in the pathogenesis of
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implicated in **benign prostatic hyperplasia**
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attractive therapeutic target.

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DN CA12610126928X

TI Treatment and prevention of prostatic disease, including prostate cancer
and **benign prostatic hyperplasia**, with
compounds binding to sex hormone-binding globulin (SHBG), and method for
therapeutic compound identification

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